Lay Abstract

Rationale:

Lung cancer (NSCLC) is the leading cause of cancer-related death in the United States. Patients with advanced lung cancer or lung cancer that has spread to other organs are currently treated with palliative chemotherapy-based treatments. With the most active chemotherapeutic agents, survival has been demonstrated to increase by several months. Clearly new therapeutic agents are needed.

The results from laboratory studies of intravenous delivery of tumor suppressor genes complexed in a fat particle (DOTAP:Chol) show reduction of experimental metastases and prolongation of survival in a mouse human lung cancer model and justify a clinical trial to assess toxicity as a prelude to possible efficacy studies. The *fus1* gene is lost in many lung cancers and when it is delivered to the cancer cell, its expression can cause cancer cell death. However, expression of *fus1* does not damage normal cells. It is likely that this gene will be deleted in the early stages of lung carcinogenesis thus making it an attractive target for all stages of disease.

Objectives:

Assess the toxicity of DOTAP:Cholesterol-fus1 Liposome Complex (DOTAP:Chol-*fus*1) administered intravenously.
To determine the maximal tolerated dose of DOTAP:Chol-*fus1* administered intravenously.
Assess the expression of *fus1* following intravenous delivery of DOTAP:Chol-*fus1* in tumor and normal cell biopsies.
Assess any anti-cancer activity for DOTAP:Chol-*fus*1.

Treatment Plan:

Patients will be given increasing doses of the liposome DNA complex containing the *fus1* gene. Toxicity will be monitored. If there is severe toxicity at any dose level, the trial will be stopped. A maximum of 30 patients will be treated in this trial. Patients may receive up to two treatments at their specified dose level. The time interval between treatments is 3 weeks. Patients will receive treatment as outpatients and will be monitored carefully after each treatment.